SCIENTIFIC LETTER

# Congestive heart failure: extent of cardiac functional changes caused by aging and organ dysfunction

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The mechanical function of the heart is known to deteriorate with increasing age and disease. After rigorous screening of necropsied hearts to exclude cardiovascular disease, Olivetti *et al*[1] in New York showed that about one third of the cardiomyocytes are lost from the human male heart between the ages of 17–90 years. This natural attrition contrasts with the loss incurred through myocardial infarction and cardiomyopathy, the most common causes of heart failure (HF) in western societies. We sought to identify whether the functional impacts of cardiac impairment through aging and HF are similar or different by conducting symptom limited cardiopulmonary exercise testing in conjunction with haemodynamic evaluations.

## METHODS

Thirty seven male subjects were recruited and assigned to the following groups. The first group (20y-Sed) consisted of sedentary untrained healthy men aged 21 (1.6) years (mean (SD), n = 12). The second group (60y-Sed) were 60 (2.9) years old (n = 14). They were screened by a medical history-lifestyle questionnaire and a treadmill ECG exercise stress test and considered to be free of overt cardiovascular disease. Subjects with any history of hypertension, diabetes, neuromuscular impairment, or cardiac or other medical conditions, or who were taking prescribed medications known to affect cardiovascular or respiratory function were excluded. The third group (60y-HF) consisted of 58.3 (3.2) year old patients with HF (n = 11). These patients were in New York Heart Association class III with impaired left ventricular systolic function and consisted of men with congestive HF secondary to idiopathic dilated cardiomyopathy and ischaemic heart disease, who were undergoing clinically indicated cardiopulmonary exercise testing with a view to estimating prognosis and considerations for interventions. This study was approved by the ethics committees of Liverpool John Moores University and the Leeds Teaching Hospitals Trust with all the subjects giving written informed consent to participate.

The same methods for cardiopulmonary exercise testing and non-invasive haemodynamic assessment as previously described were employed.[2] Briefly, an incremental exercise test on a treadmill was conducted to determine each participant's peak oxygen consumption ($Vo_{2max}$). This was done by the breath by breath gas analysis Medgraphics CPX-D system (St Paul, Minnesota, USA) to measure oxygen uptake and carbon dioxide production. Mean arterial pressure (MAP) was obtained by auscultatory sphygmomanometry and calculated according to the equation MAP = DBP + 0.412 (SBP − DBP), where DBP is systemic arterial diastolic blood pressure and SBP is systolic blood pressure.[3] Cardiac output (CO) was measured non-invasively by using the carbon dioxide rebreathing techniques of Collier and Defares and the indirect Fick method.[2] All subjects exercised on a treadmill to attain $Vo_{2max}$, when exercise peak MAP and peak CO were measured. Cardiac power output (CPO) was calculated as CPO = (CO × MAP) × K, where K is the factor ($2.22 \times 10^{-3}$) to convert units into Watts.[4] The cardiac pump functional reserve was calculated as the difference between peak CPO and CPO at rest. All data are presented as mean (SEM). Comparisons between groups were analysed by a one way analysis of variance followed by Tukey's HSD post hoc analysis.

## RESULTS

In these sedentary populations, aging (from early (20 years) to later (60 years) adulthood) resulted in a reduction of peak aerobic capacity by about 30% ($p < 0.0001$) from 43.7 (1.7) ml/kg/min (table 1). HF produced a further reduction of about 30% ($p < 0.0.001$) in aerobic exercise capacity in the same 60 year old age group (fig 1A). The most prominent difference between the impact of aging and of HF on cardiac function was their opposite effects on cardiac pressure generating capacity during peak exercise (fig 1A). The pressure generating capacity of the aging hearts was preserved and even slightly enhanced ($p < 0.01$), whereas HF significantly compromised cardiac pressure generating capacity ($p < 0.0001$). When compared with the same age group of healthy controls, HF diminished the pressure generating capacity of patients by 23.1% ($p < 0.0001$) from 128.0 (2.4) mm Hg. This diminution is not secondary to peripheral vascular resistance as fig 1B shows, where the patients with HF had significantly ($p < 0.01$) lower pressure generating capacity, most clearly seen in the overlapping ranges of systemic vascular resistance.

The flow generating capacity, on the other hand, was reduced 22% secondary to aging from 21.7 (0.6) l/min ($p < 0.0001$), with a further reduction of 26.6% due to HF ($p < 0.0001$). The power generating capacity of the heart was reduced to a smaller extent of 14.8% ($p < 0.0001$) through aging from 5.7 (0.12) W but by a much greater further reduction of 56.8% ($p < 0.0001$) by HF. The reserve capacity of the heart to impart hydraulic energy to maintain the circulation during peak physical stress was reduced by 16.5%, from 4.6 (0.13) W through aging ($p < 0.001$) and a much greater further reduction of 71.5% by HF ($p < 0.0001$).

## DISCUSSION

Patients with HF are generally affected by both the aging and disease processes. Hitherto, no study has attempted to delineate the manner in which cardiac impairment in these patients were brought about by the aging process and the disease itself. Both HF and aging reduced the cardiac flow generating capacity. However, cardiac pressure generating

**Abbreviations:** 20y-Sed, 20 year old healthy sedentary men; 60y-HF, 60 year old patients with heart failure; 60y-Sed, 60 year old healthy sedentary men; CO, cardiac output; CPO, cardiac power output; DBP, diastolic blood pressure; HF, heart failure; MAP, mean arterial pressure; SBP, systolic blood pressure; $Vo_{2max}$, peak oxygen consumption

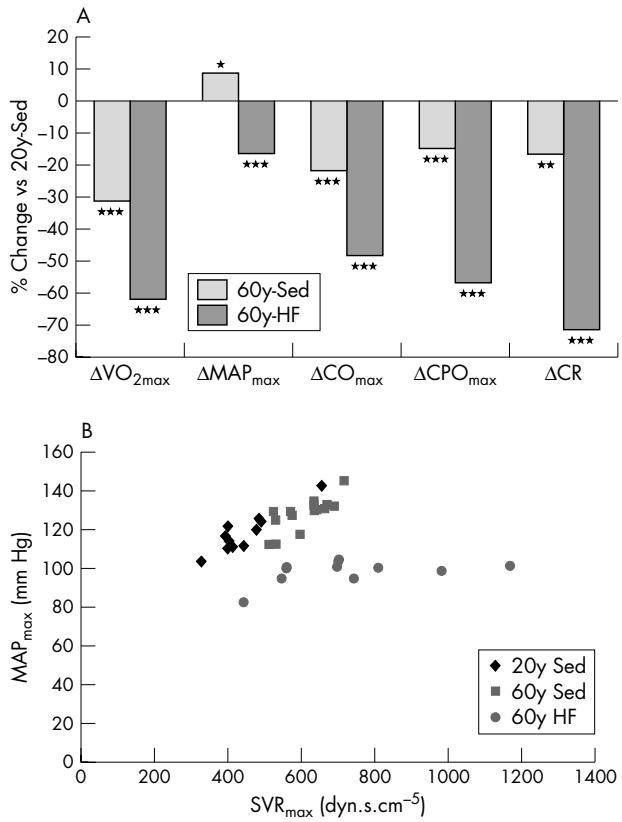


**Figure 1** Central haemodynamic parameters during peak exercise: effects of aging and heart failure. (A) Comparisons of 60 year old healthy sedentary men (60y-Sed) and 60 year old patients with heart failure (60y-HF) versus 20 year old healthy sedentary men (20y-Sed). The mean (SEM) data for 20y-Sed during maximal exercise were peak oxygen consumption ($VO_{2max}$) 43.7 (1.7) ml/kg/min, peak mean arterial pressure ($MAP_{max}$) 117.7 (3.0) mm Hg, peak cardiac output ($CO_{max}$) 21.7 (0.6) l/min, peak cardiac power output ($CPO_{max}$) 5.7 (0.12) W, and cardiac reserve (CR) 4.6 (0.13) W. *$p < 0.01$; **$p < 0.001$; ***$p < 0.0001$. (B) Relation of $MAP_{max}$ and systemic vascular resistance ($SVR_{max}$) during peak exercise in each cohort.

capacity is intact with aging but is significantly impaired with HF. The directionally opposite changes in peak MAP suggest that a proportion of cardiac work in the older healthy subjects was necessary to produce pressure work to overcome the greater systemic vascular resistance, compared with their younger counterparts (fig 1B). This type of diverting cardiac work away from flow generation during peak exercise may imply that the conventional parameters, $Vo_{2max}$ and peak CO, may actually be overestimating the cardiac deterioration due to aging. Our study also shows that by ignoring the pressure generating capacity and concentrating purely on the flow generating capacity of the heart, the diminution of peak CO underestimates the functional loss of cardiac pumping reserve secondary to HF.

A better representation of cardiac function and impairment is to combine the pressure and flow generating capacities of the heart, by considering the power generating capacity.[5] The much greater percentage loss of power in HF, concomitant with the diminution of both the flow and pressure generating capacities, indicates that disease leading to HF is more detrimental to the heart than aging, despite the apparently similar stepwise decreases (about 30%; see above) in aerobic exercise capacity by either of the two processes. The influences of medication are indeterminate in this study and hence the observations made on HF patients necessarily reflect the combined effects of disease and medication. Both aging and HF reduced peak CPO and $Vo_{2max}$, but with aging this reduction was solely due to impairment in flow generating capacity. In HF it was due to both low flow and pressure generating capacities, even though at peak exercise many of the patients with HF reached similar levels of systemic vascular resistance to non-HF subjects.

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**Table 1** Central haemodynamic parameters measured at rest and at peak exercise: effects of aging and heart failure (HF)

| | 20y-Sed (n = 12) | 60y-Sed (n = 14) | Δ *v* 20y-Sed | 60y-HF (n = 11) | Δ *v* 20y-Sed |
|---|---|---|---|---|---|
| $Vo_{2max}$ (ml/kg/min) | 43.7 (1.7)* | 30.1 (3.7)††† | −13.6 | 16.6 (3.8)‡‡‡ | −27.1 |
| $RER_{max}$ | 1.08 (0.01) | 1.07 (0.01) | 0.01 | 1.10 (0.03) | 0.02 |
| $MAP_{rest}$ (mm Hg) | 87.0 (2.4) | 102.2 (2.3)††† | 15.2 | 91.4 (2.3)‡‡ | 4.4 |
| $MAP_{max}$ (mm Hg) | 117.7 (3.0)* | 128.0 (2.4)†† | 10.3 | 98.4 (1.9)‡‡‡ | −19.3 |
| $CO_{rest}$ (l/min) | 5.5 (0.2) | 4.4 (0.2)† | −1.1 | 5.6 (0.5)‡ | 0.1 |
| $CO_{max}$ (l/min) | 21.7 (0.6)* | 17.0 (0.4)††† | −4.7 | 11.2 (0.8)‡‡‡ | −10.5 |
| $CPO_{rest}$ (W) | 1.1 (0.1) | 1.0 (0.1) | −0.1 | 1.1 (0.1) | 0.1 |
| $CPO_{max}$ (W) | 5.7 (0.1)* | 4.8 (0.1)††† | −0.8 | 2.4 (0.2)‡‡‡ | −3.2 |
| CR (W) | 4.6 (0.1)* | 3.8 (0.1)††† | −0.8 | 1.3 (0.1)‡‡‡ | −3.3 |

Data are mean (SEM).
*$p<0.001$ significant difference between 60 year old patients with HF (60y-HF) and 20 year old healthy sedentary men (20y-Sed); †$p<0.05$, ††$p<0.01$, †††$p<0.001$ 60 year old healthy sedentary men (60y-Sed) versus 20y-Sed; ‡$p<0.05$, ‡‡$p<0.01$, ‡‡‡$p<0.001$ 60y-Sed versus 60y-HF.
$CO_{max}$, peak cardiac output; $CO_{rest}$, cardiac output at rest; $CPO_{max}$, peak cardiac power output; $CPO_{rest}$, cardiac power output at rest; CR, cardiac reserve; $MAP_{max}$, peak mean arterial pressure; $MAP_{rest}$, mean arterial pressure at rest; $RER_{max}$, peak respiratory exchange ratio; $Vo_{2max}$, peak oxygen consumption.

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# IMAGES IN CARDIOLOGY

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## Cardiac sarcoidosis in a 60 year old woman

A 60 year old diabetic woman presented with atypical chest pains. Cardiac assessment did not reveal abnormalities, and the chest *x* ray was normal. Two years later she developed progressive heart failure, with mildly elevated troponin T values, and regional left ventricular (LV) wall motion abnormalities. Diagnostic coronary angiography showed mild wall irregularities. She was treated with an angiotensin converting enzyme inhibitor, a β blocker and diuretics, but her condition gradually deteriorated.

Assessment with $^{123}$fluorodeoxyglucose positron emission tomography (FDG PET) suggested active myocardial inflammation (panels A–C). Endomyocardial biopsies taken from the right ventricle (RV) were diagnostic of cardiac sarcoidosis and immunosuppressive treatment was initiated (panel D). Follow up with gadolinium cardiac magnetic resonance (CMR) after six months demonstrated extensive myocardial scarring without signs of active inflammation (panels E–G).

This case illustrates the value of PET and CMR in managing patients with cardiac sarcoidosis.

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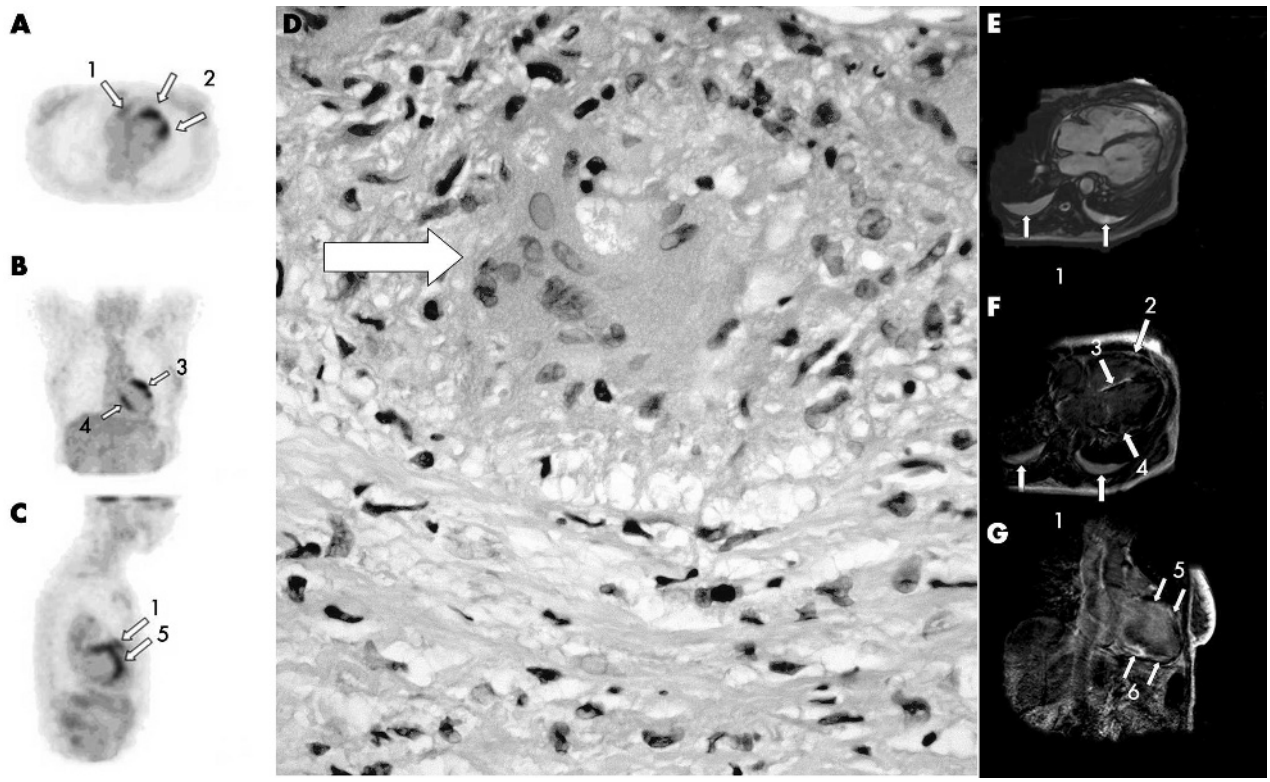


Panels A–C: $^{123}$Fluorodeoxyglucose positron emission tomography (FDG PET) demonstrates increased uptake in the right ventricular (RV) free wall (1), apex (2), and lateral (3), inferior (4) and anterior left ventricular (LV) segments (5). (A: transverse view; B: coronal view; C: sagittal view). Panel D: Photomicrograph of the endomyocardial biopsy shows the presence of a non-caseous epithelioid granuloma with a multinucleated giant cell (arrow) (haematoxylin & eosin, 40 ×). Panels E–G: Cardiac magnetic resonance (CMR) demonstrates cardiomegaly, bilateral pleural effusions (1) , and myocardial scar involving the epicardial RV free wall (2), interventricular septum (3), and subendocardium of the lateral (4) , anterior (5) and inferior LV segments (6). The RV and LV ejection fractions were respectively 15% and 22%, with 28% of the LV mass consisting of scar tissue. (E and F: four chamber views; G: two chamber view).